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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,164	11/26/2003	Stephan R. Targan	025663-001201US	8299

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EXAMINER	
ROONEY, NORA MAUREEN	
ART UNIT	**PAPER NUMBER**
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/723,164	TARGAN ET AL.	
	Examiner	Art Unit	
	NORA M. ROONEY	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,26 and 29-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-26 and 29-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01/09/2009 has been entered.

2. Claims 25-26 and 29-36 are pending and currently under consideration as they read on a method of determining a risk of having or developing a clinical subtype of Crohn's disease characterized by fibrostenosis, internal perforating disease or the need for small bowel surgery in a subject having Crohn's disease, comprising determining the presence or absence of three markers in the subject, said three markers being IgA anti-I2 antibodies, anti-Saccharomyces cerevisiae antibodies (ASCA), and IgA anti-OmpC antibodies.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 25-26 and 29-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Targan et al. (PTO-892 mailed on 01/29/2007, Reference U) in view of Vasiliauskas et al. (Reference 30, IDS filed on 11/03/2004) and Landers et al. (Reference 17, IDS filed on 11/03/2004).

Targan et al., teaches detecting the magnitude (predominant reactivity was defined as a high level of a single antibody) of anti-I2, ASCA and anti-OmpC IgA molecules in patients with ilieal or illeal with right sided colonic Crohn's disease by ELISA. The results were correlated with antibiotic induced clinical remission (a clinical subtype). The results showed that patients having anti-I2, ASCA or anti-OmpC IgA molecules were more likely to achieve antibiotic-induced clinical remission (In particular, abstract).

The claimed invention differs from the prior art by the recitation of "a clinical subtype of Crohn's disease characterized by fibrostenosis, internal perforating disease or the need for small bowel surgery" and "wherein a high magnitude of said three markers relative to levels found in individuals who do not have Crohn's disease indicates a first risk of having or developing said clinical subtype of Crohn's disease, a high magnitude of exactly two of said three markers relative to levels found in individuals who do not have Crohn's disease indicates a second risk of having or developing said clinical subtype of Crohn's disease, a high magnitude of exactly one of said three markers relative to levels found in individuals who do not have Crohn's disease indicates a third risk of having or developing said clinical subtype of Crohn's disease, and the absence of a high magnitude of said three markers relative to levels found in individuals who do

not have Crohn's disease indicates a fourth risk of having or developing said clinical subtype of Crohn's disease" and "wherein said first risk is greater than said second risk, said second risk is greater than said third risk, and said third risk is greater than said fourth risk" of claim 25; "a clinical subtype of Crohn's disease characterized by the need for small bowel surgery" "wherein a high magnitude of said three markers relative to levels found in individuals who do not have Crohn's disease indicates a first risk of having or developing said clinical subtype of Crohn's disease, a high magnitude of exactly two of said three markers relative to levels found in individuals who do not have Crohn's disease indicates a second risk of having or developing said clinical subtype of Crohn's disease, a high magnitude of exactly one of said three markers relative to levels found in individuals who do not have Crohn's disease indicates a third risk of having or developing said clinical subtype of Crohn's disease, and the absence of a high magnitude of said three markers relative to levels found in individuals who do not have Crohn's disease indicates a fourth risk of having or developing said clinical subtype of Crohn's disease" and "wherein said first risk is greater than said second risk, said second risk is greater than said third risk, and said third risk is greater than said fourth risk" of claim 26; "a clinical subtype of Crohn's disease characterized by fibrostenosis, internal perforating disease or the need for small bowel surgery" "wherein a greater magnitude of said three markers combined relative to levels found in individuals who do not have Crohn's disease indicates a greater risk of having or developing said clinical subtype characterized by fibrostenosis, internal perforating disease or the need for small bowel surgery" of claim 29; "wherein the step of determining the magnitude of three markers in the subject further comprises a step of performing quartile analysis of the magnitude of each marker" of claim 30; "wherein quartile analysis further comprises assigning

scores based on the quartile into which a marker falls and then adding the scores to obtain a quartile sum score whereby a higher quartile sum score indicates a greater risk of having or developing said clinical subtype characterized by fibrostenosis, internal perforating disease or the need for small bowel surgery" of claim 31; "a clinical subtype of Crohn's disease characterized by fibrostenosis, internal perforating disease or the need for small bowel surgery" "wherein a high magnitude of said three markers relative to levels found in individuals who do not have Crohn's disease indicates a first risk of having or developing said clinical subtype of Crohn's disease, a high magnitude of exactly two of said three markers relative to levels found in individuals who do not have Crohn's disease indicates a second risk of having or developing said clinical subtype of Crohn's disease, a high magnitude of exactly one of said three markers relative to levels found in individuals who do not have Crohn's disease indicates a third risk of having or developing said clinical subtype of Crohn's disease, and a low magnitude of said three markers relative to levels found in individuals who do not have Crohn's disease indicates a fourth risk of having or developing said clinical subtype of Crohn's disease, wherein the magnitude of each of said one or more markers is determined by contacting the sample with an antigen or fragment thereof specifically reactive with each of said one or more markers, and assaying for the magnitude of each of said one or more markers by detecting specific binding of said antigen or fragment thereof, and wherein said first risk is greater than said second risk, said second risk is greater than said third risk, and said third risk is greater than said fourth risk" of claim 32; "a clinical subtype of Crohn's disease characterized by the need for small bowel surgery" and "wherein a high magnitude of said three markers relative to levels found in individuals who do not have Crohn's disease indicates a first risk of having or developing said clinical subtype of

Crohn's disease, a high magnitude of exactly two of said three markers relative to levels found in individuals who do not have Crohn's disease indicates a second risk of having or developing said clinical subtype of Crohn's disease, a high magnitude of exactly one of said three markers relative to levels found in individuals who do not have Crohn's disease indicates a third risk of having or developing said clinical subtype of Crohn's disease, and a low magnitude of said three markers relative to levels found in individuals who do not have Crohn's disease indicates a fourth risk of having or developing said clinical subtype of Crohn's disease, wherein the magnitude of each of said one or more markers is determined by contacting the sample with an antigen or fragment thereof specifically reactive with each of said one or more markers, and assaying for the magnitude of each of said one or more markers by detecting specific binding of said antigen or fragment thereof, and wherein said first risk is greater than said second risk, said second risk is greater than said third risk, and said third risk is greater than said fourth risk" of claim 33; "a clinical subtype of Crohn's disease characterized by fibrostenosis, internal perforating disease or the need for small bowel surgery" and "wherein a greater magnitude of said three markers combined relative to levels found in individuals who do not have Crohn's disease indicates a greater risk of having or developing said clinical subtype characterized by fibrostenosis, internal perforating disease or the need for small bowel surgery" of claim 34; "wherein the step of determining the magnitude of three markers in the sample further comprises a step of performing quartile analysis of the magnitude of each marker" of claim 35; and "wherein quartile analysis further comprises assigning scores based on the quartile into which a marker falls and then adding the scores to obtain a quartile sum score whereby a higher quartile sum score indicates a

greater risk of having or developing said clinical subtype characterized by fibrostenosis, internal perforating disease or the need for small bowel surgery" of claim 36.

Vasiliauskas et al. teaches that numerous attempts have been made to characterize CD patients into uniform subgroups to better understand and predict clinical course and responses to medical and surgical interventions, particularly by serum immune markers and using selective expression of markers was demonstrated as a complementary approach for identification of immunologically and clinically homogeneous subgroups (In particular, first two paragraphs on page 487, page 493 first paragraph of the 'Discussion'). The reference teaches detecting the magnitude of ASCA and ANCA antibodies as a tool to stratify Crohn's disease into immunologically homogenous subgroups with distinct clinical characteristics including fibrostenosis, internal perforating disease and the need for small bowel surgery. ('Assessment of clinical characteristics' section pages 488-489, paragraph spanning 490-491, section spanning pages 491-493). The antibody levels were normalized and compared and statistical analysis was performed. The reference also teaches that a high magnitude of two of the markers indicates a first risk of having or developing the clinical subtype of Crohn's disease, a high magnitude of one of the markers indicates a second risk of having or developing said clinical subtype of Crohn's disease, and the absence of a high magnitude of the markers indicates a third risk of having or developing said clinical subtype of Crohn's disease (In particular, paragraph spanning page 491 to last paragraph on page 492, discussion, whole document). Marker magnitude predicted Crohn's disease clinical characteristics and the reference suggests using further

immune markers to better characterize and stratify disease subgroups (In particular, abstract, page 493, first paragraph of discussion and throughout results, page 494, last paragraph).

Landers et al. teaches detecting the magnitude of OpmC, ASCA and anti-I2 antibodies to determine the relationship of serum activity to these antigens in a clinical cohort a clinical subtype (loss of tolerance to microbial antigens). The markers were measured and quartile and cluster analysis was performed to determine the relationship between the marker antibodies in the Crohn's disease cohort (In particular, Figure 2). A number was assigned to each quartile and the sum of the quartiles was correlated to reactivity (In particular, paragraph spanning pages 693-694). The reference also teaches that a high magnitude of the three markers relative to levels found in individuals who do not have Crohn's disease indicates a first risk of having or developing the clinical subtype of Crohn's disease, a high magnitude of two of the markers relative to levels found in individuals who do not have Crohn's disease indicates a second risk of having or developing the clinical subtype of Crohn's disease, a high magnitude of one of the three markers relative to levels found in individuals who do not have Crohn's disease indicates a third risk of having or developing said clinical subtype of Crohn's disease, and the absence of a high magnitude of the three markers relative to levels found in individuals who do not have Crohn's disease indicates a fourth risk of having or developing said clinical subtype of Crohn's disease (In particular, Table 1, Figures 2-7, 'Discussion' section).

It would have been obvious to a person of ordinary skill in the art at the time the invention to combine the teachings of Targan, Landers and Vasiliauskas because all three

references are directed to measuring antibodies to bacteria associated antigens to stratify Crohn's Disease patients into clinical subtypes. It would also be obvious to analyze the data to determine risk of developing the clinical subtype based upon the magnitude of the antibodies to bacteria associated antigens. It would be obvious to determine the risk of having or developing the disease based upon the magnitude of three, two, one and no detectable antibodies to bacteria associated antigens. It would be obvious to analyze the data statistically and based on the teaching of Landers et al., it would be obvious to specifically perform quartile analysis including determining the quartile sum score to correlate the data to a clinical subtype. It would have been obvious to perform the method of determining the correlation of Crohn's disease markers anti-I2, ASCA and anti-OmpC IgA to any of the clinical outcomes of Targan et al. and Vasiliauskas et al. to obtain the claimed invention particularly since Vasiliauskas et al. teaches that numerous attempts have been made to characterize CD patients into uniform subgroups to better understand and predict clinical course and responses to medical and surgical interventions, particularly by serum immune markers and that stratification based on CD behavior has been widely studied and reported. The statistical techniques of Landers et al. including quartile analysis with quartile sum scores simply demonstrated a useful method known in the art to analyze the antibody marker magnitude and prevalence data. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Semaker. 217 USPQ 1, 5 - 6 (Fed. Cir. 1983). See MPEP 2144.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments submitted on 01/09/2009 have been fully considered, but are not found persuasive.

Applicants argue:

> "A claim is considered obvious "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a). The Supreme Court in *KSR International Co. v. Teleflex Inc.,* 550 U.S. __, __, 82 USPQ2d 1385, 1395-97 (2007) identified a number of rationales to support a conclusion of obviousness which are consistent with the proper "functional approach" to the determination of obviousness as laid down in *Graham.* The key to supporting any rejection under 35 U.S.C. § 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. The Supreme Court in *KSR* noted that the analysis supporting a rejection under 35 U.S.C. § 103 should be made explicit. One of the rationales addressed by the court in *KSR* supports a finding of obviousness when the prior art reference (or combination of references): (1) teaches or suggests the claim elements; (2) provides some suggestion or motivation to combine the references; and (3) provides a reasonable expectation of success. M.P.E.P. § 2143.
>
> The Examiner alleges that Targan *et al.* is being relied on simply for its teaching that a subset of Crohn's disease patients has the serological markers I2 and OmpC. With respect to Vasiliauskas *et al.,* the Examiner states that this reference teaches detecting ASCA and ANCA antibodies as a tool to stratify Crohn's disease into immunologically homogenous subgroups with distinct characteristics including fibrostenosis, internal perforating disease, and the need for small bowel surgery. The Examiner is of the opinion that one of ordinary skill in the art at the time of invention would have combined the OmpC and I2 markers with ASCA to further stratify the fibrostenotic subgroups, especially given the fact that some types of Crohn's disease are associated with other bacterial markers as taught by Targan *et al.* and Landers *et al.*
>
> Applicants assert that Vasiliauskas *et al.* merely teach the use of ASCA and ANCA in stratifying Crohn's disease in patients. There is certainly no mention of anti-I2 antibodies or anti-OmpC antibodies and their use in combination with ASCA to assess the risk of having or developing various Crohn's disease subtypes. In fact, Vasiliauskas *et al. teach away* from the presently claimed methods by disclosing that *all* patients with high levels of ASCA without ANCA developed fibrostenosis, with the vast majority experiencing internal penetrating complications (79%) and the need for small bowel surgery (86%). *See,*

page 492, first column and Figures 2-3. As a result, one of ordinary skill in the art would not have sought additional markers to stratify Crolm's disease into the instantly claimed clinical subtypes because Vasiliauskas *et al.* explicitly teach that high levels of ASCA were independently associated with the universal occurrence of fibrostenosis, the frequent development of internal penetrating complications, and the significantly higher need for small bowel surgery in patients without ANCA. Given the teachings in Vasiliauskas *et al.* of the diagnostic power of using solely ASCA to stratify Crohn's disease into various clinical subtypes, one of ordinary skill in the art would have understood that it is neither necessary nor beneficial to include additional markers.

Even if one of ordinary skill in the art were motivated to stratify Crohn's disease using ASCA in combination with other markers, there is simply no teaching or suggestion in any of the cited references that ASCA should be specifically combined with *both* anti-I2 and anti- OmpC antibodies. Although Targan *et al.* teach the determination of ASCA, anti-I2 antibody, anti-OmpC antibody, and ANCA levels, there is no disclosure whatsoever that high levels of one or more of these markers are associated with any Crohn's disease subtypes. Absent such a teaching in Targan *et al.* that the levels of a particular combination of markers correlate with specific Crohn's disease subtypes, one skilled in the art could have easily chosen to measure ASCA levels in combination with *either* anti-I2 antibody or anti-OmpC antibody levels, or with markers not described in the reference. As a result, Applicants assert that the Examiner has used impermissible hindsight to improperly combine specific markers taught by Targan *et al.* (anti-I2 and anti-OmpC antibodies) with a specific marker taught by Vasiliauskas *et al.* (ASCA) to arrive at the presently claimed methods. However, there is simply no rational underpinning to combine these references to support a legal conclusion of obviousness because Vasiliauskas *et al.* teach that ASCA alone is more than adequate in stratifying Crohn's disease, and Targan *et al.* fail to teach or suggest which specific marker(s) should be added to ASCA to stratify Crohn's disease if the skilled artisan were motivated to include additional markers.

Landers *et al.* does not supply the teachings that are clearly lacking in Targan *et al.* and Vasiliauskas *et al.* Rather, Landers *et al.* teach that serum immune responses to the microbial antigens ASCA, OmpC, and I2 and the autoantigen ANCA were not uniform among CD patients, but exhibited a diversity of patterns that differed widely among groups of CD patients. *See,* page 697, left column. In fact, Landers *et al. teach away* from the presently claimed methods by stating that "[t]he relationship of these different patterns of immune responses to clinical behavior is not yet clear." *See, id.* Therefore, one skilled in the art would appreciate that Landers *et al.* did not investigate, let alone identify, any associations between the different patterns of immune responses observed and specific Crohn's disease subtypes.

As with Targan *et al.,* absent such a teaching in Landers *et al.* that the levels of a particular combination of markers correlate with specific Crohn's disease subtypes, one skilled in the art could have easily chosen to measure ASCA levels as taught by Vasiliauskas *et al.* in combination with *either* anti-I2 antibody or anti-OmpC antibody levels, or with markers not disclosed in the reference. Again, Applicants assert that the Examiner has used impermissible hindsight to improperly combine specific markers taught by Targan *et al.* and Landers *et al.* (anti-I2 and anti-OmpC antibodies) with a specific marker taught by Vasiliauskas *et al.* (ASCA) to arrive at the claimed invention. However, there is simply no rational underpinning to combine these references to support a legal conclusion of obviousness because Vasiliauskas *et al.* teach that ASCA alone is more than adequate in stratifying Crohn's disease, and neither Targan *et al. nor Landers et al.* teach or suggest which specific marker(s) should be added to ASCA to stratifyCrohn's disease if the skilled artisan were motivated to include additional markers.

For the foregoing reasons, Applicants submit that the cited references, whether alone or in combination, fail to contemplate the presently claimed methods for determining a risk of having or developing a clinical subtype of Crohn's disease characterized by fibrostenosis, internal perforating disease, or the need for small bowel surgery by determining the magnitude of three specific markers: anti-I2 antibodies, ASCA, *and* anti-OmpC antibodies. "

It is the Examiner's position that the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Applicant's assertion that Vasiliauskas *et al.* merely teaches the use of ASCA and ANCA in stratifying Crohn's disease in patients but that there is certainly no mention of anti-I2 antibodies or anti-OmpC antibodies and their use in combination with ASCA to assess the risk of having or developing various Crohn's disease subtypes is not persuasive because the references are being combined for their teachings. It is obvious to measure three known serum antibodies to bacteria associated antigens to stratify disease subtypes, including anti-I2 antibodies as taught by Targan et al. . It is the Examiner's position that Vasiliauskas does not teach away from the presently claimed methods by disclosing that all patients with high levels of ASCA without ANCA developed fibrostenosis, with the vast majority experiencing internal penetrating complications and the need for small bowel surgery, contrary to Applicant's assertion. Vasiliauskas teaches that one absolutely would have sought additional markers by the teaching on page 494, last paragraph to use further immune markers to better characterize and stratify disease subgroups.

Targan *et al.* teach the determination of ASCA, anti-I2 antibody, anti-OmpC antibody, and ANCA levels and all references teach the stratification of clinical subtypes based upon antibodies to bacteria associated antigens. Contrary to Applicant's assertion all of the references teach that high levels of one or more of these markers are associated with Crohn's disease subtypes in the results sections of each reference. The references as a whole teach that it is obvious to arrive at the claimed invention. It is obvious to measure any one or combination of the antibodies to stratify clinical subtypes given the teachings of the references which all seek to

link disease with the antibody profiles. Impermissible hindsight is not the rationale being used by the Examiner. The legal test for obviousness re-iterated by Applicant in the response is that that the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Such is the instant case, it is obvious to stratify disease using known antibody markers, particularly since as taught by Vasiliauskas et al. that that numerous attempts have been made to characterize CD patients into uniform subgroups to better understand and predict clinical course and responses to medical and surgical interventions, particularly by serum immune markers and using selective expression of markers was demonstrated as a complementary approach for identification of immunologically and clinically homogeneous subgroups.

The Examiner agrees that Landers *et al.* teach that serum immune responses to the microbial antigens ASCA, OmpC, and I2 and the autoantigen ANCA were not uniform among CD patients, but exhibited a diversity of patterns that differed widely among groups of CD patients. Serum positivity to one marker indicates a small risk of having or developing a Crohn's Disease subtype of loss of tolerance to microbial antigens. The teaching in Landers *et al.* that "[t]he relationship of these different patterns of immune responses to clinical behavior is not yet clear" does not teach away. The statement supports the method of determining a relationship between disease subtype and antibodies to bacterial antigens. Clearly Landers did investigate an association between the different patterns of immune responses observed and specific Crohn's disease subtypes, as was shown in and the point of the entire reference.

The Examiner only needs to set forth a logical reason to combine the references. The reason to combine references need not be explicitly taught in the prior art, nor does the argument need to be for the same reasons that the Applicant used to invent.

5. No claim is allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

June 19, 2009

Nora M. Rooney

Patent Examiner

Technology Center 1600

/Nora M Rooney/

Examiner, Art Unit 1644